

Examiner stated that the reasons for the rejection were “essentially the same as set forth in the prior office action.” With respect to the composition claims added in the Applicants’ response to the first office action, the Examiner simply referred to Kyle, columns 13-16, where some examples of the invention in Kyle are presented.

Since the Examiner reiterates the grounds for rejection raised in the First Office Action, it is convenient to summarize those grounds here. In that action, the Examiner asserted that Kyle teaches an infant formula comprising DHA and ARA in amounts comparable to those present in human milk, and that the presence of those two acids in infant food is critical for the healthy growth of the infants. Admitting that Kyle does not teach the administration of that infant formula to preterm infants, the Examiner then asserted that Crozier et al. teach that “the presence of ARA and DHA in food is particularly important for the proper growth and development of preterm infants because they are unable to synthesize sufficient ARA and DHA.” Thus, the Examiner concluded, “it would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to employ the infant formula of Kyle to preterm infants.”

In addition, in the Final Office Action, the Examiner rejects the existence of any difference between the “proper growth” taught by Crozier et al., and the “enhanced growth” taught in the present Application, asserting that enhanced growth, as defined in the specification, “is relative to those fed with DHA only, or without DHA and ARA.” Applicants respectfully submit that the Examiner failed to appreciate the scope of the teachings in Crozier et al. and, because of that, to appreciate also the surprising results

shown in the present Application. Applicants believe that these surprising results fully rebut the obviousness grounds presented by the Examiner.

Specifically, to appreciate fully the scope of Crozier et al.'s teachings, it is appropriate to question what Crozier et al. understand as "proper growth and development of the preterm infant." The answer can be found in their own article. Specifically, on page 95, column 2, lines 1-11, the authors discuss the new understanding of the scientific community regarding the role that lipids have in cell structure and function. One aspect of this understanding, "is the contribution of nutritionally essential fatty acids to growth and function of nervous tissue in the infant."

(Emphasis supplied)

The authors then proceed to focus on the two particular acids at the center of this invention: docosahexaenoic acid (DHA) and arachidonic acid (ARA). On page 96, column 3, lines 1-22, the authors explain:

Both docosahexaenoic and arachidonic acids are important in brain growth. Brain tissue is 60% lipid and its fatty acid composition is surprisingly constant: the predominant acids are AA [ARA] and DHA.

After discussing the preterm infants' inability to synthesize DHA and ARA from their fatty acid precursors, the authors continue to explain the role of these essential fatty acids. At page 97, column 2, lines 1-21, the authors discuss the apparent effect of these acids on visual function and brain development:

Breast feeding has an effect on maturation of visual acuity. Measures of visual evoked potential and forced-choice preferential looking were significantly different in infants fed breast milk compared to those fed formula. Measures of intellectual development have also been demonstrably different between breast and formula fed preterm infants. Morley et al showed that preterm infants who had been given breast milk had better developmental scores at the age of 18 months. This advantage continued: at 7.5 to 8 years of age, the breast-fed group scored

significantly higher intelligence quotients as demonstrated by the Weschler Intelligence Scale for Children.

These quoted paragraphs clearly show that for Crozier et al. "proper growth and development of the preterm infants" means "proper growth of the nervous system and mental development of the preterm infant." Preterm infants' proper brain growth, accelerated maturation of visual acuity, and improved intellectual development are the benefits that the authors seek in promoting the addition of DHA and ARA to infants' formula. The authors, unlike Applicants, do not seek to increase the rate of weight gain in preterm infants or teach that such an increase is possible by feeding the infants DHA and ARA.

The authors of the article do not suggest that the addition of those fatty acids to the infants' food may have the effect of enhancing the infants' weight gain. To the contrary, Carlson et al.'s study found a significant drop in the studied infants' weight gain when the infants were fed with DHA from fish oil. The authors postulated that eicosapentaenoic acid (EPA), an acid that was present in the fish oil studied at an EPA to DHA ratio of 1.5:1 which competes with ARA in many biochemical reactions, may substitute for ARA in those reactions and, thus, may be responsible for the drop in weight gain. There is no suggestion or indication in Crozier et al. that the addition of ARA be made for purposes other than compensating for the drop in weight gain observed by Carlson et al. There is no teaching in Crozier et al. that an effect other than compensating for that drop in weight gain is even possible.

The present invention, on the other hand, rests on the surprising discovery that adding DHA and ARA to a preterm infant formula not only cancels the drop

in weight gain reported by Carlson et al. but also increases the weight gain to such an extent that preterm infants receiving DHA & ARA enhanced formula during their one-month hospitalization after birth and who are then switched to regular term infant formula after discharge from the hospital have, after 57 months from conception, approximately the same weight as term infants continuously breast-fed since birth.

The above-referred surprising result of Applicants' investigation is clearly shown in the Application. Specifically, in the Final Study Report, under the heading Study Objective and Statistical Analysis, Application, page 22, lines 16-29 (approximately), Applicants report the goals of their investigation as follows;

The primary objective of this study was to establish the safety of feeding D [DHA-enhanced formula] or DA [DHA & ARA-enhanced formula] to preterm infants during the initial hospitalization as measured 1) by growth, acceptance and tolerance while consuming the formula for at least 1 month and 2) by close monitoring and observation for a 4 to 5 month follow-up period (4-5 times the treatment period) while consuming unsupplemented routine term infant formula. The primary growth parameter selected was weight with evaluation of the proposition that weight on test formula was greater than or equal to weight on control formula.

Secondary objectives were 1) to evaluate the impact of fatty acid levels in erythrocyte phospholipids at the end of study feeding and 2) to determine if any effect on mean visual acuity greater than half an octave could be demonstrated at 2 and 4 months corrected age. (Emphasis supplied)

Further, at page 23, lines 7-13 of the Application, Applicants report the results as follows:

Post-hoc analysis reveals that infants on DA [DHA & ARA-enhanced formula] grew faster than infants receiving C [regular formula] and D [DHA-enhanced formula] (See table 5 and figure 1). This enhanced growth provided faster "premature infant catch-up" compared to C and D. Weight achieved by the DA group (3198 g) was higher than C (3075 g) and D (3051 g) at 40 weeks post-conceptual age but had not fully

caught up to the term weight (3438 g) of group H [breast-fed term infants] (See table 4 and figure 2). This catch up trend continued through 48 to 57 weeks by which time the mean weight of group DA did not differ from group H while groups C and D remained significantly lower.

These surprising results, wholly unexpected from the teachings in Crozier at al., clearly show that the claimed method enhances the preterm infant physical growth beyond levels achievable with formulas not supplemented with both DHA and ARA. Without these results, the person with ordinary skill in the art finds no motivation to administer the term infant formula in Kyle to preterm infants to enhance their weight gain beyond the levels achievable with unsupplemented formulas. Thus, we respectfully submit that the claimed method to enhance preterm infants' growth by administering a growth-enhancing amount of DHA and ARA is patentably distinct over the references cited by the Examiner.

In summary, in view of the foregoing arguments, we respectfully submit that the rejected claims are patentably distinct over the references cited by the Examiner and meet all other statutory requirements. We believe that the present Application is now in complete condition for allowance and, therefore, respectfully request the Examiner to reconsider the rejections in the Final Office Action and allow this Application. We invite the Examiner to telephone the undersigned should any issues remain after the consideration of this response.

Please charge any additional fees that may be required to Deposit Account No.
50-1196.

Respectfully requested,

NELSON MULLINS RILEY & SCARBOROUGH

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Date



Neil C. Jones
Registration No. 35,561

Keenan Building, Third Floor
1330 Lady Street
Columbia, SC 29201
Phone: (864) 250-2260
Fax: (803) 256-7500